
SORS: Mutations and Variations in Health and Disease: Protein Interaction Networks and 3D Structure Information

Objectives

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Abstract

In the last years Systems Biology has provided frameworks to integrate high-throughput biological and clinical data, providing significant insights into some of the fundamental roles of genes and proteins in maintaining a functional cellular state. However, it is still challenging to employ quantitative methods to identify important disease-related relationships between proteins harbouring mutations in their structural domains. In our approach we zoom in from a macroscopic view of PPI networks, and review how protein structural information can play a pivotal role in interpreting genetic variants in a PPI context. By mapping variants onto experimental structures or predicted models of protein complexes, one can offer a physico-chemical explanation of the functional impact of these variants; this may help to unravel the molecular basis of a particular disease. We then zoom out to look at how PPI data annotation and integration is essential to gain a deeper understanding of the effect of variants on PPIs communication and miscommunication. We conclude it is necessary to acquire a multidimensional view of the interaction network, in order to fully understand the role of genetic variants in health and disease.

We observe clear differences in the distribution of mutation types in different 3D-structure regions, with complementary patterns distinguishing between pathogenic and common variants, suggesting that these properties can be used as input for predictions tools. More generally, we show that 3D PPIN analysis can also help biologists to effectively search for possible targets for disease treatment.

Short bio

Prof. Franca Fraternali received her PhD in Physical Chemistry from the University of Naples, spending part of the PhD at the Polytechnic of Zurich (ETH). After post-doctoral experiences at the ETH and at the EMBL in Heidelberg, in the year 2000 she became staff scientist at the Mathematical Biology Division of the National Institute for Medical Research in London. Since 2005 she has established her own group at King's College London. In 2012 she was awarded the Chair of Bioinformatics and Computational Biology. She is member of the executive committee of the Thomas Young Centre for Simulation of Materials and co-director of the CANES CDT in Non-Equilibrium Systems at King's College London. Prof. Fraternali is Fellow of the Royal Society of Chemistry and of the Royal Society of Biology.

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Speakers

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